Author's response to reviews

Title: The natural history of pregnancies with a diagnosis of Trisomy 18 or Trisomy 13; a retrospective case series

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Author's response to reviews: see over
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Dear Sir/Madam,

Thank you for your reviews of our paper: “The natural history of pregnancies with a diagnosis of Trisomy 18 or Trisomy 13; a retrospective case series”.

Please find attached a revised manuscript. Changes in the text are highlighted in colour.

We have addressed the reviewers’ comments in detail as follows:

Review by Deborah Bruns:

Major compulsory revisions:

• It is not clear what the number of non-trisomy pregnancies were during the 2001-2012 period. This contextual data would assist interpretation of the presented prevalence data.

• This reviewer is interested in details about “A detailed structural anomaly scan was carried out in seventeen T18 (17/46; 37%) and six T13 (6/24; 25%) pregnancies to further investigate abnormalities detected on routine dating ultrasound scans” to further determine similarities and differences among the samples and existent literature. This additional data would be beneficial for readers.

The total number of live births in the region studied during the time period has been added to the paper.

Details in relation to the indications stated for structural anomaly scans performed in affected pregnancies have been mentioned. The new Table 3 shows the findings at anomaly scans in the relevant pregnancies.

Minor essential revisions:

• This reviewer asks that the authors define “consultant–led antenatal care” for those not familiar with the Irish system of health care.

• The gestation data, while helpful, does not fully describe the findings. For example, were any (all) of the earlier gestation deliveries due to a recommendation from obstetricians? This is frequently done in the United States as a frame of reference and impacts mean gestational age data.

The term “consultant-led antenatal care” has been defined in the text. The means hospital based and consultant led.
The reasons for early-gestation deliveries have been now been described in the article.

Discretionary revisions:

- Is there data available for resolution of complications? For example, did infants receive ventilation or other forms of respiratory support? This reviewer expected such data to be shared based on the Abstract.

- This reviewer is unclear what the authors mean by “Had routine screening for fetal abnormalities been offered to pregnant women, unnecessary operative deliveries for T18 and T13 fetuses may have been averted.” (ms 18-19). Does the statement imply that emergency caesarian sections are not an option for neonates with t18 and t13? Prenatal or antenatal diagnosis, why shouldn’t neonates with these conditions be given every chance for a live birth? This reviewer's opinion aside, this statement needs explanation.

- The authors state both of the following in their manuscript “Our aim was to study the natural history of pregnancies with a fetal or neonatal diagnosis of trisomies 18 and 13. In doing so, we aimed to provide clinicians with a better indication of the course of affected pregnancies, in order to assist with counselling and management and to improve the quality of care.” and “specific clinical guidelines for the management of pregnancies with a fetal diagnosis of T18 and T13 would be beneficial for healthcare professionals caring for affected pregnancies.” There is limited elaboration for clinical practice.

Information regarding neonatal intervention following birth has been added to the manuscript.

The statement “had routine screening for fetal abnormalities been offered to pregnant women, unnecessary operative deliveries for T18 and T13 fetuses may have been averted” has been rephrased. In our practice, with a diagnosis of ‘lethal’ trisomy, it would be usual to aim to avoid CS deliveries, acting in the maternal interest for future pregnancies. We state in the paper the implications for future pregnancies of managing deliveries after CS.

Additional information in relation to the aim and objectives of the study and its clinical relevance has been provided.

Review by Joan Morris:

Major compulsory revisions:

1. The manuscript has been altered to prevent repetition in the results section of details of statistical tests performed.

2. Analysis of gender of T13 infants has been performed using the exact hypothesis test with the binomial distribution.
3. Details of maternal age at delivery have been provided in the recommended format.

4. The prenatal diagnosis rates of trisomy 18 and trisomy 13 in women who had a structural anomaly scan during their pregnancy have been provided.

5. The quoted paragraph has been rephrased as suggested.

6. The quoted phrase has been edited to avoid repetition.

7. The numbers of T18 and T13 cases have been added to Table 2.

8. An additional table (Table 3) has been provided which only contains details of anomalies in fetuses who underwent detailed structural anomaly scans. We have mentioned in the paper the limitation of the numbers who had detailed scans. It is worth re-iterating there is no national policy in Ireland on prenatal screening and diagnosis, which leads to varying rates of offer, availability and uptake of all tests. Nonetheless, we believe this important to report in entirety.

9. The total numbers of live births for each trisomy have been provided in Figure 3.

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